PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application

Brockhaus et al.

Group 1816
Examiner D. Adams

Serial No. 08/444,493, filed May 19,1995

For: HUMAN TNF RECEPTOR

DECLARATION OF DR. RICHARD A. CHIZZONITE

I, DR. RICHARD A. CHIZZONITE, a United States of America citizen and resident of South Kent, Connecticut, declare as follows:

In 1968, I received a Bachelor of Science Degree in Biology/Chemistry from Union College, Schenectady, New York.

In 1978, I received a Ph.D. in Pharmacology and Toxicology from the University of Rochester, School of Medicine and Dentistry, Rochester, New York where I carried out research in isolation and characterization of various proteins, including enzymes for neuromuscular functions.

From 1978 to 1982, I was a Research Fellow in the Department of Medicine, University of Chicago, Chicago, Illinois carrying out research c ncentrated on isolating, identifying and characterizing of IgG monoclonal antibodies.

From 1982 until the present, I have been employed in the Departments of Molecular Genetics and Inflammation/Autoimmune Diseases of Hoffmann-La Roche Inc., Nutley, New Jersey ("Roche") where I currently hold the positions of Research Leader and Project Leader of the Signal Transduction Inhibitor Project.

During my employment at Roche, my scientific duties have included studying the nature of, and characterization of, numerous proteins, including monoclonal antibodies. I have isolated and characterized monoclonal antibodies for numerous therapeutic targets, including IL-1, IL-2, IL-12, IgE, and their respective receptors. During this period, I have also cloned, expressed and characterized these therapeutic targets as recombinant proteins.

For the past two and one-half years I have developed and expressed recombinant immunoglobulin fusion proteins for therapeutic targets, such as receptors which include Type I and Type II IL-1 receptors and IL-1 receptor accessory proteins.

This Declaration is submitted to demonstrate that with respect to DNA encoding human IgG, the portion described as encoding all domains, except the first domain, of the constant region of the heavy chain of human immunoglobulin IgG is the same as that portion of DNA described as encoding a Fc portion and hinge region of an IgG heavy chain polypeptide.

Enclosed PCT International Publication No. WO 89/02922 (Exhibit A) on page 1 shows the structure of the constant domains of an IgG immunoglobulin that includes CH1,

hinge, CH2, and CH3, where CH1, CH2 and CH3 designate, respectively, the first, second, and third constant domains.

As shown in Exhibit A, when referring to an immunoglobulin, the portion designated as containing all constant domains except the first domain of the constant region of the heavy chain of human immunoglobulin IgG consists of the hinge, CH2, and CH3. Since the Fc portion of a human immunoglobulin IgG commonly refers to the portion of the immunoglobulin containing the CH2 and CH3 domains, the Fc portion plus the hinge region includes hinge, CH2, and CH3.

Therefore, a Fc portion and hinge region of an IgG heavy chain polypeptide designates all constant domains except for the first domain of the constant region of the heavy chain of human IgG immunoglobulin.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date August 2, 1996 Richard A. Chizzonite

Richard A. Chizzonite

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